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Synthesis and Structure of Fused *N*-Heterocylic Carbenes and Their Rhodium Complexes

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New procedures for the synthesis of *N* – heterocyclic carbenes with with multiple fused rings have been developed utilizing a key ring-closing metathesis step. Rhodium complexes were obtained via the pentafluorophenyl carbene adducts. Solid-state structural behavior of the new carbene ligands were analyzed via X-ray crystallography.

N–heterocyclic carbenes (NHCs), first isolated by Arduengo et al. in 1991, have become a well-studied and well-utilized class of ligands in the field of transition metal-catalyzed reactions.[1] Their proficiency in catalysis, variable electronic properties, and ease of translation into complex architectural structures have allowed for the development of unique reactivity and targeted selectivity.[2–6] In the past 20 years, NHCs have been applied as ligands in reactions such as palladium catalyzed cross-coupling, olefin metathesis, asymmetric hydrosilylation and conjugate addition.[7–12] Free NHCs have also shown great efficacy as organocatalysts in a variety of reactions.[13,14] Exploration of novel structural motifs has enabled the development of novel applications for NHCs. Serving as a positive feedback loop, as the synthetic and catalytic applications have grown, the array of structural motifs has grown in parallel (Figure 1), illustrating the dynamic interchange between structure and function.[1,15,16]

In particular, fused NHC structures are of interest, as it has been shown computationally that the rotational lability of the carbene can greatly influence the behavior and dynamics of the NHC-bound metal complex.[17,18] In this study, the syntheses of fused carbenes **6** and **7** were designed to allow for control of stereochemistry at the backbone of the NHC as well as facile modification of the N-bound arene fragment. A three-carbon chain from the backbone of the NHC to the aryl was chosen to form the cis-fused as well as the trans-fused structures (Figure 2). Independent synthesis of each carbene precursor allowed for separate cis and trans routes, bypassing a need to separate the meso from the racemic forms. Synthesis of the racemate could be easily modified to render the enantioenriched mixtures of the trans species via resolution with inexpensive L-(+)-tartaric acid.[19]

Hermann and Blechert have synthesized similar NHC structures.[16,20,21] Carbene **4** was appended to ruthenium and shown to have limited metathesis activity.[16] Unfortunately, the synthesis of **4** yielded a 3:1 mixture of the meso and racemic forms, and only the meso form was isolated for study.[16] The crystal structure of carbene **4**, which contains a C_2 linkage, exhibited planarity of the *N*-bound arene with the heterocycle, thereby rendering the ruthenium species noncanonical with standard ruthenium-based catalysts.

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Supporting Information Available. Crystallographic data for complexes **17** and **18**, experimental procedures and NMR data for all new compounds are available.

In designing both syntheses, we chose to utilize a ring closing metathesis as the key step in fusing the seven-membered ring fragment. Previous syntheses of fused NHC frameworks began from quinoline-type derivatives and were thus limited in both ring-size and stereocontrol.[16] With intimate knowledge of the olefin metathesis reaction at hand, we imagined separate syntheses hinging upon retention of the initially introduced backbone stereochemistry during ring closing metathesis (RCM).

The cis-cyclohexenyldiamine was synthesized by a known procedure.[22] Palladium catalyzed cross-coupling of the free diamine with *o*-bromostyrene yielded secondary diamine **8**. Attempts at ring-closing metathesis of **8** resulted in decomposition of both diamine and the ruthenium benzylidene species. In order to cloak the diamino functionality, **8** was condensed with pentafluorobenzaldehyde to form **9**, following a recent report.[23] Ring-closing with ruthenium catalyst provided cis-fused adduct **10** and hydrogenation gave the desired carbene precursor **11**.

Entry into the racemic trans-fused carbene began with aza-Claisen rearrangement of commercially available *N*-allylaniline. Condensation with glyoxal yielded the bisimine, which was further functionalized via Grignard addition and in situ urea formation to give intermediate **12**. Although the pentaflurophenyl adduct could be introduced immediately succeeding addition of Grignard, the urea provided higher yields in the metathesis reaction, yielding ring-closed **13**.

Hydrogenation with Pd/C at 1 atm gave the urea **14,** which was readily cleaved with lithium aluminum hydride to afford trans-fused diamine **15**. The free diamine was then condensed with pentafluorobenzaldehyde to provide the carbene precursor **16**.

Recently, we reported the facile decomposition of pentaflurophenyl adducts as NHC-precursors for ruthenium complexes.[23] We chose to isolate the masked carbene as pentaflurophenyl adducts rather than the traditional imidazolinium salts in order to allow ligation onto metal fragments in the absence of a strong base. Thus, reaction of **11** or **16** with rhodium cyclooctadiene chloride dimer gave the corresponding rhodium complexes shown (Scheme 3). Crystals suitable for X-ray diffraction studies were obtained as bright yellow blocks by vapor diffusion of pentane into a benzene solution of either **17** or **18**.

Figure 3 shows the ORTEP diagram of the cis-fused rhodium complex **17** obtained from X-Ray diffraction. We were surprised to note that, although there exists a cis-orientation at the backbone of the NHC, a distortion in the carbene allows the two linkers to obtain a relative trans configuration of the N-bound arenes. Note the dihedral torsion angle between C(12)-C(2)-C(3)-C(13) at 37.57° confirms a cis-orientation (Table 1). Neither arene is orthogonal to the plane of the NHC, containing dihedral angles at C(5)-C(4)- N(1)-C(1) of 67.86° and at C(20)-C(21)-N(2)-C(1) of 31.84°.

X-ray crystal analysis of trans-fused **18** confirmed the expected anti-anti relationship. Analogous to previously reported nonfused ligated NHCs, Figure 4 shows the NHC to be planar, without the distortion noted in Figure 3.

Table 2 lists selected bond lengths and angles for **18**. Here the dihedral torsion angle at the backbone of the carbene is greater than 90°, with the angle at C(12)-C(2)-C(3)-C(13) of 136.83°. Again, neither arene ring is orthogonal or planar to the NHC, with dihedral angles at C(5)-C(4)- N(1)-C(1) of 50.98° and at C(20)-C(21)-N(2)-C(1) of 62.57°.

A simplified side view of both cis and trans fused Rh-species with hydrogens omitted for clarity is shown in Figure 5. It is clear that the cis linkage exists for complex **17**, however,

the arenes are locked in a relative trans conformation, similar to that of complex **18**, which shows a higher degree of overall symmetry.

In summary, we have developed the synthesis of stereochemically defined fused *N*-heterocyclic carbene structures which can be obtained in gram quantities either as the meso form or the racemate. X-ray crystallography data confirmed the covalent linkages.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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References

1. Arduengo AJ, Harlow RL, Kline M. J Am Chem Soc 1991;113:361.
2. Dixon DA, Arduengo AJ. J Phys Chem 1991;95:4180.
3. Diez-Gonzalez S, Marion N, Nolan SP. Chem Rev 2009;109:3612. [PubMed: 19588961]
4. Corberan R, Mas-Marza E, Peris E. Eur J Inorg Chem 2009:1700.
5. Lee HM, Lee CC, Cheng PY. Curr Org Chem 2007;11:1491.
6. Herrmann WA, Schutz J, Frey GD, Herdtweck E. Organometallics 2006;25:2437.
7. Schwab P, France MB, Ziller JW, Grubbs RH. Angew Chem Int Ed 1995;34:2039.
8. Trnka TM, Grubbs RH. Acc Chem Res 2001;34:18. [PubMed: 11170353]
9. Herrmann WA. Angew Chem Int Ed 2002;41:1290.
10. Crudden CM, Allen DP. Coord Chem Rev 2004;248:2247.
11. Snead DR, Seo H, Hong S. Curr Org Chem 2008;12:1370.
12. de Fremont P, Marion N, Nolan SP. Coord Chem Rev 2009;253:862.
13. Enders D, Balensiefer T. Acc Chem Res 2004;37:534. [PubMed: 15311952]
14. Brown MK, May TL, Baxter CA, Hoveyda AH. Angew Chem Int Ed 2007;46:1097.
15. Berlin JM, Campbell K, Ritter T, Funk TW, Chlenov A, Grubbs RH. Organic Letters 2007;9:1339. [PubMed: 17343392]
16. Vehlow K, Gessler S, Blechert S. Angew Chem Int Ed 2007;46:8082.
17. Clavier H, Correa A, Cavallo L, Escudero-Adan EC, Benet-Buchholz J, Slawin AMZ, Noaln SP. Eur J Inorg Chem 2009:1767.
18. Ragone F, Poater A, Cavallo L. J Am Chem Soc 2010;132:4249. [PubMed: 20205432]
19. Schanz HJ, Linseis MA, Gilheany DG. Tetrahedron-Asymmetry 2003;14:2763.
20. Herrmann WA, Baskakov D, Herdtweck E, Hoffmann SD, Bunlaksananusorn T, Rampf F, Rodefeld L. Organometallics 2006;25:2449.
21. Baskakov D, Herrmann WA, Herdtweck E, Hoffmann SD. Organometallics 2007;26:626.
22. Witiak DT, Rotella DP, Filippi JA, Gallucci J. Journal of Medicinal Chemistry 1987;30:1327. [PubMed: 3612684]
23. Blum AP, Ritter T, Grubbs RH. Organometallics 2007;26:2122.

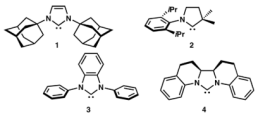


Figure 1.
NHCs utilized in metal-mediated catalysis.

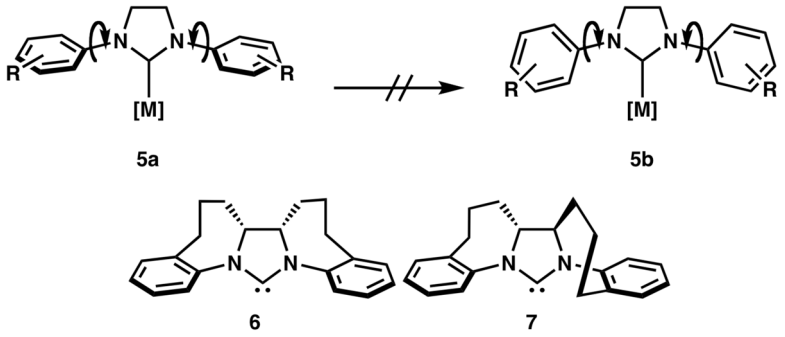


Figure 2.
Design of Rotationally Locked NHCs

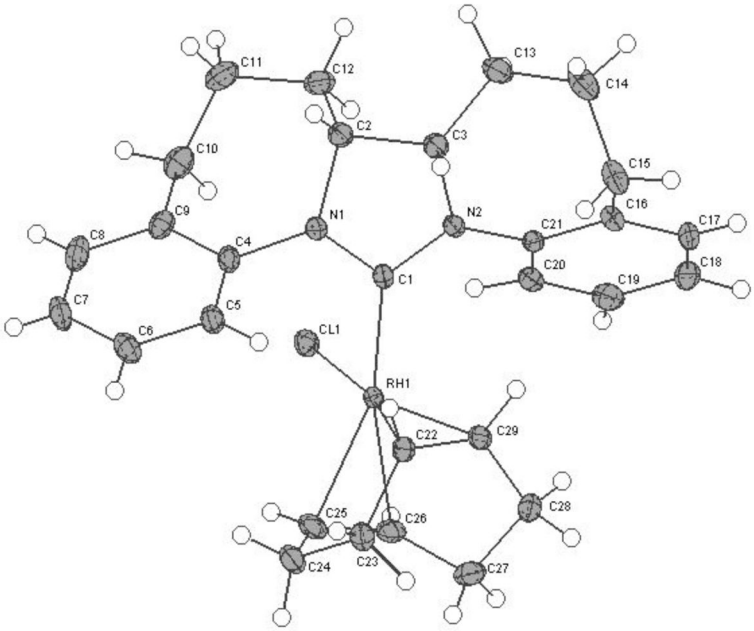


Figure 3.
ORTEP diagram of **17** with 50% probability ellipsoids.

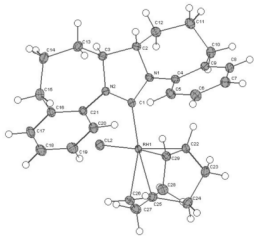


Figure 4.
ORTEP diagram of **18** with 50% probability ellipsoids.

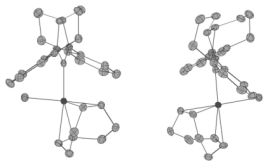
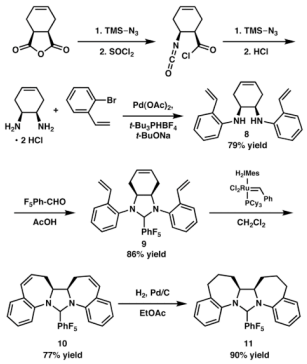
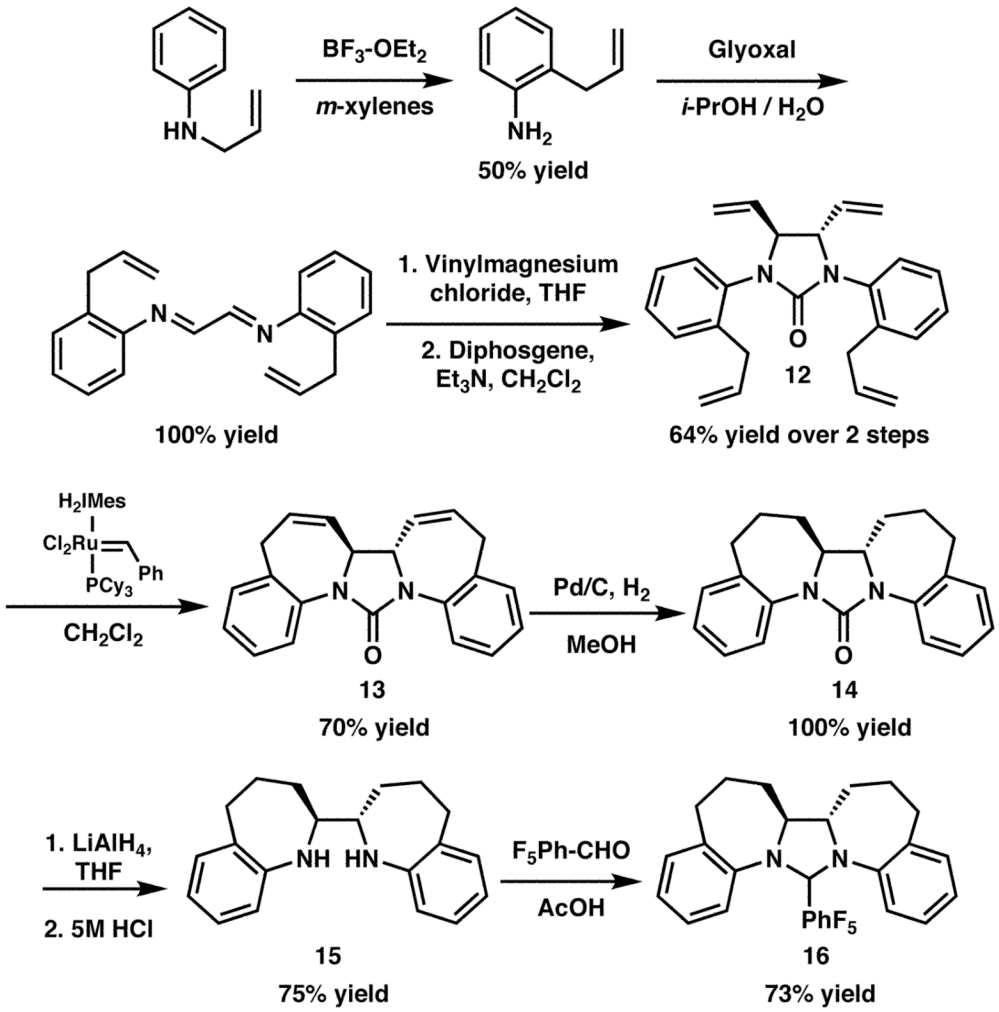


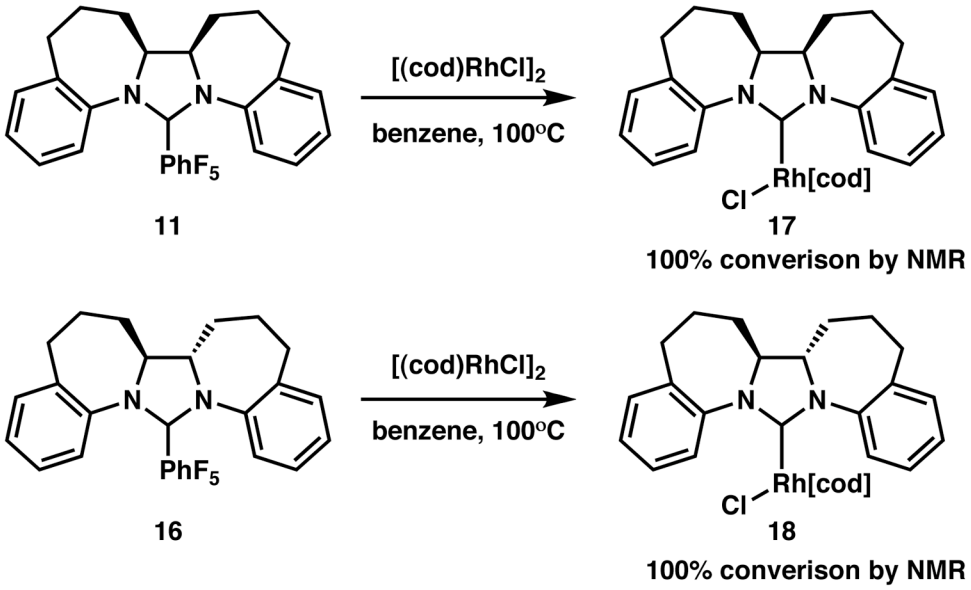
Figure 5.
Side-view of structures **17** and **18**.



Scheme 1.
Synthesis of cis carbene precursor **11**.



Scheme 2.
Synthesis of trans carbene precursor **16**.



Scheme 3.
Synthesis of rhodium complexes.

Table 1

Selected Bond Lengths [Å] and Angles [°] for **17**.

Rh(1)-C(1)	1.992(2)	C(1)-N(1)-C(2)	111.93(17)
Rh(1)-C(29)	2.105(2)	C(1)-N(2)-C(3)	110.99(17)
Rh(1)-C(22)	2.124(2)	N(1)-C(1)-N(2)	106.57(19)
Rh(1)-C(25)	2.207(2)	N(1)-C(1)-Rh(1)	124.58(14)
Rh(1)-C(26)	2.247(2)	N(2)-C(1)-Rh(1)	128.82(15)
Rh(1)-Cl(1)	2.4075(5)	N(1)-C(2)-C(3)	98.93(17)
		N(2)-C(3)-C(2)	100.04(18)
		C(12)-C(2)-C(3)-C(13)	37.57
		C(5)-C(4)-N(1)-C(1)	67.86
		C(20)-C(21)-N(2)-C(1)	31.84

Table 2

Selected Bond Lengths [Å] and Angles [°] for **18**.

Rh(1)-C(1)	2.0032(7)	C(1)-N(1)-C(2)	113.12(5)
Rh(1)-C(22)	2.0969(7)	C(1)-N(2)-C(3)	113.17(5)
Rh(1)-C(29)	2.1263(8)	N(1)-C(1)-N(2)	107.40(6)
Rh(1)-C(26)	2.1847(8)	N(1)-C(1)-Rh(1)	123.40(5)
Rh(1)-C(25)	2.2169(8)	N(2)-C(1)-Rh(1)	129.10(5)
Rh(1)-Cl(1)	2.3896(2)	N(1)-C(2)-C(3)	101.40(6)
		N(2)-C(3)-C(2)	101.27(5)
		C(12)-C(2)-C(3)-C(13)	136.83
		C(5)-C(4)-N(1)-C(1)	50.98
		C(20)-C(21)-N(2)-C(1)	62.57